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10/630,626	07/30/2003	Gregory A. Demopulos	PH.1.0037.US2	9065

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EXAMINER	
ALSTRUM ACEVEDO, JAMES HENRY	
ART UNIT	**PAPER NUMBER**
1616	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/630,626	DEMOPULOS ET AL.	
	Examiner	Art Unit	
	James H. Alstrum-Acevedo	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/4/06*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28,55 and 56* is/are pending in the application.

4a) Of the above claim(s) *4,5,9,17,18,20,22,25 and 27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6-8,10-16,19,21,23,26,28,55 and 56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/4/06; 1/3/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-28 and 55-56 are pending. Claims 55-56 are new. Previously, Applicants cancelled claims 29-54. Applicants have amended claims 1 and 28. **Claims 1-3, 6-8, 10-16, 19, 21, 23, 26, 28, and 55-56 are under consideration in the instant office action.** Claims 4-5, 9, 17-18, 20, 22, 25, and 27 are withdrawn from consideration as being drawn to a non-elected species. Receipt and consideration of Applicants' amended claim set, new IDS's (submitted 12/4/2006 and 1/3/2007), and remarks/arguments submitted on December 4, 2006 are acknowledged.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 6-8, 10-16, 19, 21, 23, 26, 28, and 55-56 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibition of pain, effecting mydriasis, and/or decreasing the intraocular pressure during an ophthalmologic procedure, does not reasonably provide enablement for treating or inhibiting inflammation generally. The specification does not enable any physician skilled in the art of medicine, to use the invention commensurate in scope with these claims.

An analysis based upon the Wands factors is set forth below.

To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. In

Genentech Inc. v. Novo Nordisk 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997); *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993),. See also *Amgen Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir. 1991); *In re Fisher* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Further, in *In re Wands* 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court stated:

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman (230 USPQ 546, 547 (Bd Pat App Int 1986)). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Breadth of Claims/Nature of the invention

Applicants' claims are broad. Applicants are claiming the inhibition of any kind of inflammation. Furthermore, the claims do not specify where the inflammation occurs, although it may occur in the ocular tissues the claim langauge does not limit the treatment of inflammation to inflammation of the eyes. The time period for the treatment of inflammation is perioperatively, which means the inhibition of inflammation continues until a patient is discharged from a hospital, or in other words the time period for the inhibition of inflammation may occur long after the ophthalmologic procedure has finished.

State of the Prior Art

Firstly, for a compound or genus to be effective against inflammation **generally** is contrary to medical science. Inflammation is a process that can take place in virtually

any part of the body. There is a vast range of forms that it can take, causes for the problem, and biochemical pathways that mediate the inflammatory reaction. There is no common mechanism by which all, or even most, inflammations arise. Mediators include bradykinin, serotonin, C3a, C5a, histamine, leukotrienes, cytokines, and many, many others (Kuby, J. Immunology, 3rd edition, W. H. Freeman and Company: New York, 1997, pp 67, 365-378). Accordingly, treatments for inflammation are normally tailored to the particular type of inflammation present, as there is no, and there can be no "magic bullet" against inflammation generally.

Inflammation is the reaction of vascularized tissue to local injury; it is the name given to the stereotyped ways tissues respond to noxious stimuli. These occur in two fundamentally different types. Acute inflammation is the response to recent or continuing injury (Kuby, J. Immunology, 3rd edition, W. H. Freeman and Company: New York, 1997, pp 370-373). The principal features are dilatation and leaking of vessels, and recruitment of circulating neutrophils. Chronic inflammation or "late-phase inflammation" is a response to prolonged problems, orchestrated by T-helper lymphocytes (Kuby, J. Immunology, 3rd edition, W. H. Freeman and Company: New York, 1997, pp 373-375). It may feature recruitment and activation of T- and B-lymphocytes, macrophages, eosinophils, and/or fibroblasts. The hallmark of chronic inflammation is infiltration of tissue with mononuclear inflammatory cells. Granulomas are seen in certain chronic inflammation situations. They are clusters of macrophages that have stuck tightly together, typically to wall something off. Granulomas can form with foreign bodies such as aspirated food, toxocara, silicone injections, and splinters.

Blepharitis is a chronic inflammation of the eyelids that is caused by a staphylococcus (see Merck Manual Home Edition article entitled, "Blepharitis"). Dacryocystitis is inflammation of the tear sac, and usually occurs after a long-term obstruction of the nasolacrimal duct and is caused by staphylococci or streptococci (see Merck Manual Home Edition article entitled, "Dacroycystitis"). Preseptal cellulitis is inflammation of the tissues around the eye, and Orbital cellulitis is an inflammatory process involving the layer of tissue that separates the eye itself from the eyelid (see Merck Manual Home Edition article entitled, "Infections"). These life-threatening infections usually arise from staphylococcus. Hence, these types of inflammations are treated with antibiotics.

Cholecystitis is gallbladder inflammation usually caused by a gallstone that cannot pass through the cystic duct (see Merck Manual Home Edition article entitled, "Cholecystitis"). In those cases, it normally cannot be treated by pharmaceuticals but instead the gallbladder is removed. Cholecystitis without the formation of gallstones, called acalculous cholecystitis, is caused by bacteria such as Salmonella, Staphylococcus, Streptococcus (as part of scarlet fever), and leptospirosis, and thus may be treatable by treating the underlying infectious agent. Acute inflammation of the gall bladder can also arise from typhoid; treatment is with antibiotics.

In gout, joint inflammation is caused by the formation of monosodium urate monohydrate (MSU) crystals within the joint space (see Merck Manual Home Edition article entitled, "Gout"). Acute attacks of gout are treated with colchicine (to inhibit of MSU-induced chemotactic factor release by PMNs) and after the acute phase with allopurinol to control the blood levels of uric acid. Pseudogout, sometimes referred to as calcium pyrophosphate disease (CPPD), is inflammation caused by calcium

pyrophosphate (CPP) crystals (see Merck Manual Home Edition article entitled, "Pseudogout"). It is treated with nonsteroidal anti-inflammatory drugs, corticosteroids, and colchicine.

Sinusitis is the inflammation of the mucosal lining of one or more sinuses. It commonly accompanies upper respiratory viral infections and in most cases requires no treatment (see Merck Manual Home Edition article entitled, "Sinusitis").

Pharyngitis (tonsillitis) is an inflammatory illness of the mucous membranes and underlying structures of the throat (nasopharynx, uvula, and soft palate) (see Merck Manual Home Edition article entitled, "Pharyngitis"). The illness can be caused by bacteria, viruses, mycoplasmas, fungi, and parasites, and uncertain causes, especially Streptococcus pyogenes, adenoviruses, influenza viruses, parainfluenza viruses, Epstein-Barr virus, enteroviruses, and Mycoplasma pneumoniae. Similarly, Osteomyelitis is the inflammation of bones, generally caused by bacteria (most commonly Staphylococcus Aureus). Fungi or viruses can cause the disease. Dacryoadenitis (see Merck Manual Home Edition article entitled, "Inflammation"), an inflammation of the tear gland, can arise from infectious mononucleosis, mumps, gonorrhea, or influenza. Conjunctivitis (pink eye) is inflammation of the conjunctiva and can be caused by many microorganisms, including staphylococci, Haemophilus influenzae, streptococci, gonococci, and viruses such as adenoviruses (see Merck Manual Home Edition article entitled, "Conjunctivitis"). Treatment in all of these cases, when possible, is thus to the underlying infectious agent.

Rheumatoid arthritis is an inflammatory bone disease causing destruction of articular cartilage, in which macrophages accumulate in the rheumatoid synovial

membrane (see Merck Manual Home Edition articles entitled, "Reiter's Syndrome" and "Rheumatoid Arthritis"). Mediators are cytokines, including IL-18 and IL-18, and IFN- .

Pneumonia is an inflammation of the lungs that can be caused by viruses (such as respiratory syncytial, parainfluenza, and influenza), bacteria, fungi, mycoplasmas, rickettsias (especially Q fever), Chlamydia, or parasites (see Merck Manual Home Edition article entitled, "Eosinophilic Pneumonia"). It can also occur as a hypersensitivity, or allergic response, to agents such as mold, humidifiers, and animal excreta, and in such a case would be treated with anti-allergic agents.

Other inflammations in the respiratory system include CF, adult respiratory distress syndrome, asthma, and bronchitis.

Myocarditis is an inflammation of the muscular middle layer of the heart (myocardium) Viruses, bacteria, and noninfectious diseases can cause it. Treatment is primarily supportive e.g. drugs may be used to improve the heart's ability to contract and to remove extra fluids from the body. Unless the underlying infectious agent itself is treatable, this inflammation is not itself treated.

Glossitis is inflammation of the tongue (see Merck Manual Home Edition article entitled, "Tongue Disorders"). Local causes of glossitis include bacterial or viral infection, mechanical irritation or injury from burns, rough edges of teeth or dental and oral appliances, or other trauma; exposure to irritants (tobacco, alcohol, hot foods, or spices), and sensitization (to e.g. toothpaste, mouthwash, breath fresheners, dyes in candy, plastic in dentures or retainers) anemia and other B vitamin deficiencies, erythema multiform, pemphigus vulgaris, syphilis, and other disorders. It can be inherited. Corticosteroids such as prednisone may be given to reduce the inflammation.

Antibiotics, antifungal medications, or other antimicrobials may be prescribed if the cause of glossitis is an infection. Anemia and nutritional deficiencies must be treated, often by dietary changes or other supplements.

Meningitis is an inflammation of the outer covering of the brain and spinal cord (see Merck Manual Home Edition article entitled, "Meningitis"). Virtually any known infectious agent can cause it. Thus, if it were caused by Haemophilus influenzae or Neisseria meningitis, the antibiotic derivative rifampin would be used.

Encephalitis is an inflammation of the brain itself. It is most often caused by a group of arboviruses (see Merck Manual Home Edition article entitled, "Viral Infections"). Treatment of encephalitis is largely supportive because no specific antiviral agents, except for that which works against herpes simplex virus, are available for therapy.

Hepatitis is an inflammation of the liver, usually caused by viral invasion, notably hepatitis A, B and C, but sometimes Epstein-Barr virus; herpes simplex viruses; measles, mumps, and chicken pox viruses; and cytomegaloviruses. Treatment, when possible, is with antivirals. Inflammation of the liver also takes the form of alcoholic hepatitis. Lupoid hepatitis is an autoimmune disorder.

Hemorrhoids are an enlarged or varicose condition of the hemorrhoidal veins and tissues around the anus, either internal or external (see Merck Manual Home Edition article entitled, "Hemrroids"). Anything that obstructs the free circulation of the blood in the portal system will give rise to hemorrhoids. Constipation, straining at stool, diarrhea, dysentery, rough toilet paper, uncleanness, pelvic tumors, displacement of the uterus and pregnancy are among the most common causes.

There is a series of inflammatory problems directly connected to neutrophil-endothelial cell adhesion (NECA). These include frostbite injury, bacterial meningitis, acute airway inflammation, allograft rejection, hemorrhagic shock, septic shock, ischemia, and reperfusion injuries.

Urethritis is an inflammation of the duct that leads from the bladder to the exterior of the body (see Merck Manual Home Edition article entitled, "Urethritis"). It is often due to fecal contamination or irritation due to physical or chemical substances (e.g. introduction of foreign bodies into the urethra, bubble bath, or soap) or gonorrhea. Treatment may simply involve the withdrawal of the offending chemical agent, or the administration of antibiotics, when Neisseria gonorrhoeae is involved.

Inflammation can arise from the eruption of teeth in a child (teething).

Inflammation of the nails can arise from chronic paronychia, fungus (especially Candida albicans), trauma, impaired circulation, and dermatitis.

Bright's disease (or glomerulonephritis) is inflammation of the glomeruli and the nephrons, the structures in the kidney that produce urine. It usually results from an infection, such as a streptococcal infection, that occurs somewhere else in the body. There is no real treatment beyond relief of the symptoms.

Thyroiditis is an inflammation of the thyroid gland, and takes three forms. Hashimoto's Thyroiditis (chronic lymphocytic thyroiditis) is the most common type of thyroiditis. It is an autoimmune disorder, and treatment is to start thyroid hormone replacement. For De Quervain's Thyroiditis (subacute or granulomatous thyroiditis), treatment is usually bed rest and aspirin to reduce inflammation. Occasionally cortisone

and thyroid hormone may be used. Silent Thyroiditis usually arises following pregnancy. Treatment is usually bed rest with beta-blockers.

Regional enteritis (Crohn's disease or ileitis) is an autoimmune disorder, which is associated with the presence of Mycobacterium paratuberculosis. It can affect any part of the gastrointestinal tract but most commonly affects the ileum. The inflammation is controlled primarily by regulation of diet, antibiotics if abscesses and fistulas are present, sometimes Prednisone and other corticosteroids, and surgery.

Stomatitis, inflammation of the mouth, and mucositis, inflammation of the mucosa can arise from sources as diverse as Candida albicans, dentures, chemotherapy, and radiation therapy to the head, neck or mouth ("Radiation mucositis"). It may be secondary to infection, trauma, systemic diseases or autoimmune mechanisms. These come in many forms, such as aphthous ulcers, Acute Necrotizing Ulcerative Gingivitis i.e. "trench mouth", and Lichen Planus. Herpetiform ulcers treatment has ranged from antibiotics, immunosuppressants and yogurt, to Lactobacillus capsules, tetracycline and systemic steroids. Palliative measures include topical anesthetics, Vitamin E, analgesics, and coating agents. Antiviral agents may be used if viral origin is established.

Pancreatitis is inflammation of the pancreas and can arise from abdominal trauma, or the formation of gallstones that obstruct the common bile duct. It can be associated with excessive ingestion of alcohol; with disorders such as cystic fibrosis or Reye's syndrome; or with scorpion stings. Infectious causes include mycoplasmas, Epstein-Barr viruses, Coxsackie viruses, leptospirosis, hepatitis viruses, mumps, congenital German measles, Ascaris worms, and syphilis. The inflammation per se is generally not treatable.

Treatment is usually supportive and consists of the management of pain and intravenous feeding.

Neuroretinitis is inflammation of the retina and optic nerve of the eye ("optic neuritis") (see printout of medline plus definition). It is often idiopathic. It frequently arises secondary to some kind of infection, such as Hepatitis B, HSV, EBV, influenza A, mumps, Coxsackie B, TB, salmonella, Lyme disease, syphilis, leptospirosis, Histoplasmosis, Toxoplasmosis, toxocara, Sarcoidosis, and cat-scratch disease. Treatment is thus to the underlying cause. For example, diffuse unilateral subacute neuroretinitis (DUSN) arises from nematodes deep in the retina or in the subretinal space. Anthelminthic treatment is then used. When the origin is Toxoplasmosis, then anti-Toxoplasma medications such as Pyrimethamine.

Other eye inflammations include scleritis and episcleritis (see Merck Manual Home Edition articles entitled, "Scleritis" and "Episcleritis"), inflammation of tissues on the sclera; choroiditis, inflammation of the middle coat (choroid) of the eyeball, and uveitis (see Merck Manual Home Edition article entitled, "Uveitis"), which is inflammation of the parts of the eyes that make up the iris (see also Merck Manual Home Edition article entitled, "Inflammation").

Gastritis is inflammation to the stomach lining. Atrophic gastritis is characterized by the loss of the stomach cells that are responsible for manufacturing acid, pepsin, and intrinsic factor. This condition occurs in older people or those suffering from Helicobacter pylori. Erosive (hemorrhagic) gastritis occurs when shallow ulcers or sores develop on the upper layer of the stomach lining, usually because of the excessive ingestion of a stomach irritant such as aspirin or alcohol.

There can also be mentioned appendicitis, which can occur when a hard piece of stool blocks the opening of the appendix, causing swelling and inflammation.

The great majority of skin problems involve some type of inflammation, such as response to physical injury (e.g. sunburn, ticks, abrasion, or a bee string), acute allergic contact dermatitis (such as poison ivy), and infections (such as boils and cold sores). Ingrown hairs, or pili incarnati, can cause acute pustular reactions. Cancerous lesions of the skin frequently show some degree of inflammatory response. The inflammation of acne is caused by leakage of sebum and keratin debris outside the distended pilosebaceous duct. The bacillus Propionibacterium acnes, which populate the lesions, may also contribute indirectly to this inflammation by metabolizing the sebum to produce irritant fatty acids. Inflammation in skin problems is usually the result of the release of chemical mediators in the skin, notably histamine, peptides (kinins) and fatty acids (prostaglandins and leukotrienes), that are formed enzymatically in response to e.g. injury. Medications designed to counteract inflammation in the skin may or may not antagonize the effects of the particular type of mediator involved, if that is known. The inflammation can take many different forms, including redness, (from dilation of blood vessels); heat, (from increased blood flow); swelling (from leakage of fluid from the small blood vessels); whealing reactions (hives, nettle rash, urticaria) in which vascular changes predominate, and pain or itching. Blisters (from enzymes released from inflammatory cells, resident cells of the skin, or blood plasma components) can cause the breakdown of proteins responsible for the structural integrity of the skin, leading to serious inflammatory disorders such as pemphigus. In addition, the affected skin may feel indurated (hardened) because of the deposition of the coagulation protein fibrin and

the infiltration by inflammatory blood cells (lymphocytes, histiocytes, and polymorphonuclear leukocytes).

Prostatitis, inflammation of the prostate, comes in several different forms, including those of bacterial origins, and those, which are not, including chronic abacterial prostatitis and asymptomatic inflammatory prostatitis. Certain types of anti-inflammatory agents, such as non-steroidal anti-inflammatory medications (Ibuprofen and naproxen) along with muscle relaxants can be used in the non-bacterial cases.

The above list is by no means complete, but demonstrates the extraordinary breadth of causes, mechanisms, and treatment (or lack thereof) for inflammation. It establishes that it is not reasonable for any agent to be able to treat or inhibit inflammation generally.

Level of One of Ordinary Skill & Predictability/Unpredictability in the Art

The level of a person of ordinary skill in the art is high, with ordinary artisans having advanced medical and/or scientific degrees (e.g. M.D., Ph.D., Pharm. D. or combinations thereof). There is a general lack of predictability in the pharmaceutical art. *In re Fisher*, 427, F. 2d 833, 166, USPQ 18 (CCPA 1970).

Guidance/Working Examples

The instant specification provides several examples (Examples 1-3), which provide guidance for the local treatment of inflammation in the ocular tissues during various ophthalmologic procedures (e.g. cataract surgery and trabulectomy), utilizing specific anti-inflammatory agents (i.e. ketoprofen, flurbiprofen, and or prednisolone).

The specification describes various anti-inflammatory agents (e.g. serotonin receptor antagonists), but does not indicate or provide guidance as to when one would choose a particular anti-inflammatory agent or how one would select one or more anti-inflammatory agents from the 11 different types of anti-inflammatory agent classes described in the specification.

In summary, the Examiner concludes that the cited claims are not enabled for the general inhibition of inflammation perioperatively during an ophthalmologic procedure, but are enabled for the inhibition of pain, effecting mydriasis, and/or decreasing the intraocular pressure during an ophthalmologic procedure.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 1-3 and 12-15 under 35 U.S.C. 102(b) as being anticipated by Cagle et al. (WO 95/16435; IDS) **is withdrawn** per Applicants' claim amendments requiring that one of the two agents be either a mydriatic agent or an intraocular pressure (IOP) reducing agent.

Response to Arguments

Applicant's arguments, see page 8, filed December 4, 2006, with respect to the rejection of claims 1-3 and 12-15 under 35 U.S.C. 102(b) as being anticipated by Cagle et al. have been fully considered and are persuasive. The rejection of claims 1-3 and 12-15 under 35 U.S.C. 102(b) as being anticipated by Cagle et al. has been withdrawn.

The rejection of claims 1, 6, and 8 under 35 U.S.C. 102(b) as being anticipated by Gan et al. (U.S. Patent No. 5,523,316; IDS) **is withdrawn** per Applicants' claim amendments requiring that one of the two agents be either a mydriatic agent or an intraocular pressure (IOP) reducing agent.

Response to Arguments

Applicant's arguments, see page 8, filed December 4, 2006, with respect to the rejection of claims 1, 6, and 8 under 35 U.S.C. 102(b) as being anticipated by Gan et al. (U.S. Patent No. 5,523,316; IDS) have been fully considered and are persuasive. The rejection of claims 1, 6, and 8 under 35 U.S.C. 102(b) as being anticipated by Gan et al. (U.S. Patent No. 5,523,316; IDS) has been withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue; and resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejection of claims 1-3, 6-8, 10-16, 19, 23, 26, and 28 under 35 U.S.C. 103(a) as being unpatentable over Thomas (U.S. Patent No. 5,811,446) **are withdrawn**, per Applicants' persuasive arguments that Thomas teaches away from continuous irrigation.

Response to Arguments

Applicant's arguments, see pages 10-12, filed December 4, 2006, with respect to the rejection of claims 1-3, 6-8, 10-16, 19, 23, 26, and 28 under 35 U.S.C. 103(a) as being unpatentable over Thomas (U.S. Patent No. 5,811,446) have been fully considered and are persuasive. The rejection of claims 1-3, 6-8, 10-16, 19, 23, 26, and 28 under 35 U.S.C. 103(a) as being unpatentable over Thomas (U.S. Patent No. 5,811,446) has been withdrawn.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the

unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The rejections on the ground of nonstatutory obviousness-type double patenting of claims 1 and 28 as being unpatentable over (1) claims 1-4 of U.S. Patent No. 6,056,715 (USPN '715); (2) claims 1-3 of U.S. Patent No. 5,820,583 (USPN '583); and (3) claims 1-3 of U.S. Patent No. 6,210,394 (USPN '394) **are withdrawn** per Applicants' claim amendments requiring that one of the two agents be either a mydriatic agent or an intraocular pressure (IOP) reducing agent.

Response to Arguments

Applicant's arguments, see page 12-13, filed December 4, 2006, with respect to the rejections on the ground of nonstatutory obviousness-type double patenting of claims 1 and 28 as being unpatentable over (1) claims 1-4 of U.S. Patent No. 6,056,715 (USPN '715); (2) claims 1-3 of U.S. Patent No. 5,820,583 (USPN '583); and (3) claims 1-3 of

U.S. Patent No. 6,210,394 (USPN '394), all in view of Thomas et al. (U.S. Patent No. 5,811,446) have been fully considered and are persuasive.

Claims 1 and 28 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over (1) claims 1-12 and 18 of U.S. Patent No. 6,261,279 (USPN '279); (2) claims 18-20 of U.S. Patent No. 6,413,961 (USPN '961); and (3) claims 12-17 and 23-28 of U.S. Patent No. 6,420,432 (USPN '432) all in view of Revision of Pharmacology ("ROP"; New IDS reference) for the reasons of record set forth on pages 12-13 of the office action mailed on June 1, 2006. The cited U.S. Patents lack the express teaching of methods wherein at least one agent is a mydriatic agent or an intraocular pressure-increasing agent. This deficiency is cured by the teachings of ROP that anti-histamines dilate capillaries, which would obviously result in mydriasis when applied directly to ocular tissues, such as in claims 1 and 28 of the instant application. For these reasons, an ordinary skilled artisan would conclude that claims 1 and 28 of the instant application are *prima facie* obvious over the cited claims of USPN '279, USPN '961, and USPN '432.

Response to Arguments

Applicant's arguments filed December 4, 2006 have been fully considered but they are not persuasive. Applicants' traversal of these rejections is based on their assertion that the cited claims of the issued patents do not teach methods wherein at least one of the two agents is either a mydriatic agent or an IOP reducing agent. The Examiner

respectfully disagrees, because the application of anti-histamines locally to ocular tissue during an ophthalmologic procedure would result in mydriasis.

The rejection on the ground of nonstatutory obviousness-type double patenting of claims 1 and 28 as being unpatentable over claim 1 of U.S. Patent No. 6,254,585 (USPN '585) is **withdrawn** per Applicants' claim amendments requiring that one of the two agents be either a mydriatic agent or an intraocular pressure (IOP) reducing agent.

Response to Arguments

Applicant's arguments, see page 12-13, filed December 4, 2006, with respect to the rejection on the ground of nonstatutory obviousness-type double patenting of claims 1 and 28 as being unpatentable over claim 1 of U.S. Patent No. 6,254,585 (USPN '585) have been fully considered and are persuasive. The rejection on the ground of nonstatutory obviousness-type double patenting of claims 1 and 28 as being unpatentable over claim 1 of U.S. Patent No. 6,254,585 (USPN '585) has been withdrawn.

Conclusion

Claims 1-3, 6-8, 10-16, 19, 21, 23, 26, 28, and 55-56 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is

(571) 272-5548. The examiner can normally be reached on M-F, 9:00-6:30, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0664. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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